General

Guideline Title

Guidelines for the management of absolute cardiovascular disease risk.

Bibliographic Source(s)

National Vascular Disease Prevention Alliance. Guidelines for the assessment of absolute cardiovascular disease risk. Canberra (Australia): National Stroke Foundation (Australia); 2012 May. 123 p. [359 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Vascular Disease Prevention Alliance. Guidelines for the assessment of absolute cardiovascular disease risk. Canberra (Australia): National Heart Foundation of Australia; 2009. 49 p. [118 references]

Recommendations

Major Recommendations

These recommendations are from the guideline's "Summary of Recommendations" with more detailed information in the original guideline document.

Definitions for the grades of recommendations (A-D) and for consensus-based recommendations (CBR), and practice points (PP) are provided at the end of the "Major Recommendations" field. Some recommendations have been drawn from the *Guidelines for the Assessment of Absolute Cardiovascular Disease Risk* and have been included to provide context and a complete set of absolute cardiovascular disease risk recommendations. These recommendations are dated (2009) to indicate that they were developed in a separate process.

Evidence-Based Recommendations (EBR)

Assessment of Cardiovascular Disease (CVD) Risk

Clinically Determined High Risk

EBR 1: Adults with any of the following conditions do not require absolute cardiovascular risk assessment using the Framingham Risk Equation because they are already known to be at clinically determined high risk of CVD (Grade: D [2009] [National Vascular Disease Prevention Alliance, 2009]):

i. Diabetes and age >60 years
ii. Diabetes with microalbuminuria (>20 mcg/min or urinary albumin:creatinine ratio [UACR] >2.5 mg/mmol for males, >3.5 mg/mmol for

females)

iii. Moderate or severe chronic kidney disease (CKD) (persistent proteinuria or estimated glomerular filtration rate [eGFR] <45 mL/min/1.73 m^2)
iv. A previous diagnosis of familial hypercholesterolaemia
v. Systolic blood pressure (SBP) ≥180 mmHg or diastolic blood pressure (DBP) ≥110 mmHg
vi. Serum total cholesterol (TC) >7.5 mmol/L.

General Population Aged 45–74 Years

EBR 2: Absolute CVD risk assessment, using the Framingham Risk Equation to predict risk of a cardiovascular event over the next five years, should be performed for all adults aged 45–74 years who are not known to have CVD or to be at clinically determined high risk. (Grade: B [2009] [National Vascular Disease Prevention Alliance, 2009])

Aboriginal and Torres Strait Islander Adults Aged 35–74 Years

EBR 3: In Aboriginal and Torres Strait Islander adults aged 35–74 years who are not known to have CVD or to be at clinically determined high risk, absolute cardiovascular risk over the next five years should be calculated using the Framingham Risk Equation. Although the Framingham Risk Equation might underestimate risk in this population, available evidence suggests that this approach will provide an estimate of minimum cardiovascular risk. (Grade: D [2009] [Wang & Hoy, 2005])

Adults with Diabetes

EBR 4: In adults with diabetes aged 60 years or less who are not known to have CVD or to be at clinically determined high risk, absolute cardiovascular risk over the next five years should be assessed using the Framingham Risk Equation. Although the Framingham Risk Equation might underestimate risk in this population, available evidence suggests that this approach will provide an estimate of minimum cardiovascular risk. (Grade: C [2009] [National Vascular Disease Prevention Alliance, 2009])

Adults Who Are Overweight or Obese

EBR 5: In adults who are overweight or obese and who are not known to have CVD or to be at clinically determined high risk, absolute cardiovascular risk over the next five years should be assessed using the Framingham Risk Equation. The results should be interpreted with the awareness that its predictive value has not been specifically assessed in this population (Grade: D [2009] [National Vascular Disease Prevention Alliance, 2009])

Treatment

Lifestyle Modification

EBR 6: Weight loss should be recommended for people who are overweight or obese. (Grade: B [Flores-Mateo et al., 2006; Dickinson et al., 2006; Avenell et al., 2004; Hession et al., 2009])

EBR 7: All adults should be advised to participate in at least 30 minutes of moderate intensity activity on most days or preferably every day of the week. (Grade: B [Katzmarzyk et al., 2009; Hamer & Chida, 2008; Lollgen, Bockenhoff, & Knapp, 2009; Nocon et al., 2008; Shiroma & Lee, 2010])

EBR 8: All smokers should be advised to stop smoking. (Grade: A [Scottish Intercollegiate Guidelines Network (SIGN), 2007; Thomas, Elliott, & Naughton, 2006])

Pharmacotherapy

EBR 9: Aspirin or other antiplatelet therapy is not routinely recommended for primary prevention of CVD. (Grade: B [van Dis et al., 2009; "Collaborative overview," 1994; Antithrombotic Trialists' Collaboration, 2002; Berger et al. 2006; Calvin et al., 2009])

For Adults at High Risk of CVD

EBR 10: Adults at high absolute risk of CVD should be simultaneously treated with lipid and blood pressure-lowering pharmacotherapy in addition to lifestyle intervention unless contraindicated or clinically inappropriate. (Grade: B [Law, Morris, & Wald, 2009; Turnbull et al., 2005; United States National Heart, Lung, and Blood Institute, 2002; Brugts et al., 2009; Ray et al., 2010])

Blood Pressure-lowering Therapy

EBR 11: Treatment should begin with any one of the following agents (Grade: A [Law, Morris, & Wald, 2009; Wright & Musini, 2009]):

- Angiotensin-converting enzyme (ACE) inhibitor
- Angiotensin receptor blocker
- Calcium channel blocker
- Low dose thiazide or thiazide-like diuretic

EBR 12: If monotherapy does not sufficiently reduce blood pressure add a second agent from a different pharmacological class. (Grade: A [Law, Morris, & Wald, 2009])

Lipid-lowering Therapy

EBR 13: Statins should be used as first-line therapy. (Grade: A [Brugts et al., 2009; Taylor et al., 2011; Cholesterol Treatment Trialists' (CTT) Collaboration et al., 2010)

EBR 14: If low-density lipoprotein cholesterol (LDL-C) levels are not sufficiently reduced on maximally tolerated dose of statin, one or more of the following may be added:

- Ezetimibe (Grade: C [Mikhailidis et al., 2007; Ara et al., 2008; Baigent et al., 2011])
- Bile acid binding resin (Grade: D [Studer et al., 2005; Lipid Research Clinics Program, 1984])
- Nicotinic acid (Grade: D [Robinson et al., 2009; Birjmohun et al., 2005])

EBR 15: Where statins cannot be tolerated at all, one or more of the following can be used:

- Ezetimibe (Grade: D [Ara et al., 2008])
- Bile acid binding resin (Grade: D [Lipid Research Clinics Program, 1984])
- Nicotinic acid (Grade: D [Birjmohun et al., 2005; "Clofibrate and niacin in coronary heart disease," 1975; Canner et al., 1986])

EBR 16: If triglyceride levels remain elevated, treatment with one of the following may be considered:

- Fenofibrate (especially if high-density lipoprotein [HDL] is below target) (Grade: C [Law, Wald, & Thompson, 1994; Neaton et al., 1992; Smith et al., 1992; Stamler, Wentworth, & Neaton, 1986; United States National Heart, Lung, and Blood Institute, 2002; Graham et al., 2007; Brugts et al., 2009; Ray et al., 2010; Taylor et al., 2011; Cholesterol Treatment Trialists' (CTT) Collaboration et al., 2010; Thavendiranathan et al., 2006; Ward et al., 2007; Delahoy et al., 2009; Amarenco & Labreuche, 2009; Henyan et al., 2007; O'Regan et al., 2008; Corvol et al., 2003; Law, Wald, & Rudnicka, 2003; Robinson et al., 2009; Studer et al., 2005; Saha et al., 2007; Jun et al., 2010; Alleman et al., 2006])
- Nicotinic acid (Grade: C [Robinson et al., 2009; Birjmohun et al., 2005])
- Fish oil (Grade: C [Hartweg et al., 2008; Hooper et al., 2004; Yokoyama et al., 2007])

Populations Requiring Special Consideration

People with Diabetes

EBR 17: Blood pressure-lowering therapy in people with diabetes should preferentially include an ACE inhibitor or angiotensin receptor blocker. (Grade: A [Haller et al., 2011; Zoungas et al., 2009; Strippoli, Craig, & Craig, 2005; Strippoli et al., 2006])

EBR 18: If monotherapy does not sufficiently reduce blood pressure add one of the following:

- Calcium channel blocker (Grade: B [Weber et al., 2010; Ostergren et al., 2008])
- Low-dose thiazide or thiazide-like diuretic (Grade: C [Patel et al., 2007; Weber et al., 2010)

People with Chronic Kidney Disease (CKD)

EBR 19: Blood pressure-lowering therapy in people with CKD should begin with an ACE inhibitor or angiotensin receptor blocker. (Grade: A [Strippoli, Craig, & Craig, 2005; Strippoli et al., 2006])

Consensus-Based Recommendations (CBR)

Assessment of CVD Risk

General Population Aged over 75 Tears

CBR 1: In adults over 74, who are not known to have CVD or to be at clinically determined high risk, absolute cardiovascular risk over the next five years should be assessed using the Framingham Risk Equation. Calculation should be performed using the age of 74 years. Although the Framingham Risk Equation might underestimate risk in this population, available evidence suggests that this approach will provide an estimate of minimum cardiovascular risk.

Aboriginal and Torres Strait Islander Adults Aged over 74 Years

CBR 2: Aboriginal and Torres Strait Islander adults aged over 74 years should be considered as being at high CVD risk.

Treatment

For Adults at Moderate Risk of CVD

CBR 3: Adults at moderate absolute risk of CVD should have their risk factors initially managed by lifestyle interventions. Pharmacotherapy for blood pressure and/or lipid lowering is not routinely recommended but may be considered if 3 to 6 months of lifestyle intervention does not reduce the individual's risk factors.

CBR 4: Adults at moderate absolute risk of CVD may be treated with pharmacotherapy for blood pressure and/or lipid lowering in addition to lifestyle intervention if one or more of the following applies:

- Persistent blood pressure ≥160/100 mmHg
- Family history of premature CVD
- Aboriginal and Torres Strait Islander peoples
- Other populations where Framingham Risk Equation is known to underestimate risk (South Asians, Maori and Pacific Islanders, people from the Middle East)

For Adults at Low Risk of CVD

CBR 5: Pharmacotherapy for blood pressure and lipid lowering is not routinely recommended for adults at low absolute risk of CVD.

CBR 6: Adults at low absolute risk of CVD who have persistent blood pressure ≥160/100 mmHg may be treated with blood pressure-lowering pharmacotherapy in addition to lifestyle intervention.

Maximising the Benefits of Pharmacotherapy

CBR 7: Pharmacotherapy for blood pressure-lowering should aim towards the following targets while balancing the risks/benefits:

- ≤140/90 mmHg for adults without CVD (including those with CKD)
- ≤130/80 mmHg for adults with micro or macro albuminuria (UACR >2.5 mg/mmol in males and >3.5 mg/mmol in females)
- ≤130/80 mmHg for all adults with diabetes

CBR 8: Pharmacotherapy for lipid lowering should aim towards the following targets while balancing the risks/benefits:

- TC <4.0 mmol/L
- High-density lipoprotein cholesterol (HDL-C) ≥1.0 mmol/L
- LDL-C <2.0 mmol/L
- Non HDL-C <2.5 mmol/L
- Triglycerides <2.0 mmol/L

Practice Points (PP)

Assessment of CVD Risk

Conducting a Comprehensive Risk Assessment

PP 1 (2009): In adults without known CVD, a comprehensive assessment of cardiovascular risk includes consideration of the following:

Modifiable Risk Factors

- Smoking status
- Blood pressure
- Serum lipids

- Waist circumference and body mass index (BMI)
- Nutrition
- Physical activity level
- Alcohol intake

Non-modifiable Risk Factors

- Age and sex
- Family history of premature CVD
- Social history including cultural identity, ethnicity and socioeconomic status

Related Conditions

- Diabetes
- Chronic kidney disease (albuminuria ± urine protein, eGFR)
- Familial hypercholesterolaemia
- Evidence of atrial fibrillation (history, examination, electrocardiogram)

Absolute CVD Risk Categories

PP 2 (2009): The following qualitative risk categories can be used to describe calculated absolute cardiovascular risk:

- Low risk corresponds to <10% probability of CVD within the next five years
- Moderate risk corresponds to 10% to 15% probability of CVD within the next five years
- High risk corresponds to >15% probability of CVD within the next five years

All Adults Aged over 74 Years

PP 3: In adults aged over 74 years, the decision to initiate therapy should be based on clinical judgement which takes into account:

- Likely benefits and risks of treatment
- Life expectancy, co-morbidities and quality of life
- Personal values

Adults with Depression

PP 4: Adults being assessed for CVD risk should also be assessed for depression (and other psychosocial factors). Cardiovascular risk assessment using the Framingham Risk Equation may underestimate risk in adults with depression.

Socioeconomic Status

PP 5 (2009): A comprehensive assessment of cardiovascular risk involves consideration of socioeconomic deprivation, because it is an independent risk factor for CVD. Absolute risk of CVD calculated using the Framingham Risk Equation is likely to underestimate CVD risk in socioeconomically disadvantaged groups.

Atrial Fibrillation (AF)

PP 6 (2009): In adults with AF (particularly those aged over 65 years), the increased risk of cardiovascular events and all-cause mortality, in addition to thromboembolic disease including stroke, should be taken into account when assessing cardiovascular risk.

Review of CVD Risk

PP 7 (2009): Regular review of absolute cardiovascular risk is recommended at intervals according to the initial assessed risk level:

- Low – review every 2 years
- Moderate – review every 6 to 12 months
- High – review according to clinical context

PP 8: In adults at low absolute risk of CVD, blood test results within five years may be used for review of absolute cardiovascular risk unless there are reasons to the contrary.

Treatment

Lifestyle Modification

PP 9: All adults should be supported to follow the current *Dietary Guidelines for Australian Adults*.

PP 10: All smokers should be offered advice about methods to aid smoking cessation, including counselling services, and if assessed as nicotine dependent, nicotine replacement therapy or other appropriate pharmacotherapy should be used.

PP 11: All adults should be advised to follow the current *Australian guidelines to reduce health risks from drinking alcohol* (National Health and Medical Research Council, 2009).

PP 12: Adults at higher absolute risk of CVD should be given more frequent and sustained lifestyle advice, support and follow-up to achieve behavioural change.

Blood Pressure-lowering Therapy

PP 13: If blood pressure is not responding to pharmacotherapy, reassess for:

- Non-adherence
- Undiagnosed secondary causes for raised blood pressure
- Hypertensive effects of other drugs
- Treatment resistance due to sleep apnoea
- Undisclosed use of alcohol or recreational drugs
- Unrecognised high salt intake (particularly in patients taking ACE inhibitors or angiotensin receptor blockers)
- "White coat" raised blood pressure
- Technical factors affecting measurement
- Volume overload, especially with CKD

PP 14: If dual therapy at higher doses does not sufficiently reduce blood pressure, add an additional agent.

PP 15: If combination therapy does not sufficiently reduce blood pressure, consider specialist advice.

PP 16: Treatable secondary causes for raised blood pressure should be considered before commencing blood pressure drug therapy.

PP 17: The following combinations should generally be avoided:

- Potassium-sparing diuretic plus either ACE inhibitor or angiotensin receptor blocker
- Beta-blocker plus verapamil

Lipid-lowering Therapy

PP 18: Treatable secondary causes of dyslipidaemia should be considered before commencing lipid-lowering pharmacotherapy.

Maximising the Benefits of Pharmacotherapy

PP 19: Adults who commence pharmacotherapy should have their medication adjusted as required and response assessed regularly (approximately 6-12 weekly) until sufficient improvement has been achieved or maximum tolerated dose has been reached.

PP 20: Reduction or withdrawal of pharmacotherapy may be considered in adults who make sustained lifestyle changes which significantly reduce their risk (e.g., smoking cessation, significant weight loss).

Definitions:

Grading of Evidence-based Recommendations (EBR)

Grade of Recommendation	Description
A	Body of evidence can be trusted to guide practice.
B	Body of evidence can be trusted to guide practice in most situations.
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application.
D	Body of evidence is weak and recommendation must be applied with caution.

Grade of Recommendation	Description

Additional Guidance

CBR	Consensus-based recommendations: developed by the guidelines expert working group when a systematic review of the evidence found either an absence of direct evidence which answered the clinical question or poor quality evidence, which was deemed not to be strong enough to formulate an evidence-based recommendation.
PP	Practice points: developed by the guidelines expert working group where a systematic review had not been conducted but there was a need to provide practical guidance to support the implementation of the evidence-based and/or consensus-based recommendations.

Clinical Algorithm(s)

The original guideline document contains the following clinical algorithms:

- Risk Assessment and Management Algorithm: Adults Aged 45 Years and Over without Known History of CVD
- Risk Assessment and Management Algorithm: Aboriginal and Torres Strait Islander Adults Aged 35 Years and Over without a Known History of CVD

Scope

Disease/Condition(s)

Cardiovascular disease (CVD), including coronary heart disease (CHD), stroke, peripheral arterial disease, and renovascular disease

Guideline Category

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Cardiology

Endocrinology

Family Practice

Geriatrics

Internal Medicine

Nephrology

Neurology

Nutrition

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Pharmacists

Physician Assistants

Physicians

Public Health Departments

Utilization Management

Guideline Objective(s)

- To consolidate a number of evidence-based guidelines for conditions with similar risk factors and management approaches, and provide clear guidance to prevent first-ever cardiovascular disease (CVD) events
- To provide health system policy makers with the best available evidence as a basis for population health policy

Target Population

Australian adults aged 45 years and over (35 years for Aboriginal and Torres Strait Islander peoples) who have no previous history of cardiovascular disease (CVD)

Interventions and Practices Considered

Risk Assessment

1. Assessment of cardiovascular disease (CVD) risk using the Framingham Risk Equation
2. Comprehensive risk assessment of modifiable and non-modifiable risk factors and related conditions
3. Categorization according to absolute CVD risk (low, moderate, high)
4. Considerations for special patient groups: Aboriginal and Torres Strait Islanders, adults with diabetes, adults with chronic kidney disease (CKD), adults who are overweight or obese, adults over 74 years, adults with depression, adults with atrial fibrillation, and economically disadvantaged groups

Treatment/Prevention

1. Lifestyle modification (weight loss, exercise, stopping smoking)
2. Aspirin and other antiplatelet therapy (not recommended for primary prevention)
3. Establishing blood pressure and lipid targets based on risk
4. Blood pressure-lowering therapy
    - Angiotensin-converting enzyme (ACE) inhibitor
    - Angiotensin receptor blocker

    - Calcium channel blocker
    - Low-dose thiazide or thiazide-like diuretic
5. Lipid-lowering therapy
    - Statins
    - Ezetimibe
    - Bile acid binding resin
    - Nicotinic acid
    - Fenofibrate
    - Fish oil
6. Monitoring response to therapy

Major Outcomes Considered

- Cardiovascular events (primary outcome for each question)
- Absolute risk reduction (secondary outcome)
- Surrogate outcomes such as individual risk factor reduction (e.g., blood pressure control)

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The systematic literature review was undertaken according to the process outlined in the *National Health and Medical Research Council (NHMRC) Standards and Procedures for Externally Developed Guidelines* (2007) by an external group from the International Centre for Allied Health Evidence (iCAHE), University of South Australia.

Searches were conducted in relevant databases using an agreed search protocol which lists details of search terms, inclusion/exclusion criteria, and data extraction and appraisal methodology. Additional hand searching was conducted by the National Stroke Foundation (NSF) project team in several key journals to identify any major trials or meta-analyses published after the systematic literature review.

Criteria for Considering Studies for the Review

Search Dates

The search dates were 2006 to June 2010 for the first five questions relating to assessment of cardiovascular disease (CVD) risk which updated the search conducted for the *Clinical Guidelines for the Assessment of Absolute Cardiovascular Disease Risk* (which used no limits on the date of publication). The search dates were 2002 to June 2010 for the remaining questions relating to management of absolute CVD risk. Hand searching was conducted between June 2010 and May 2011 (see Appendix 2 of the original guideline document for a complete list of the questions posed for this guideline).

Types of Studies

Existing guidelines, systematic reviews (Level 1 evidence, based on the *NHMRC Levels of Evidence and Grades for Recommendations for Developers of Guidelines [2009]*), randomised controlled trials (Level II evidence) were considered for inclusion, crossing intervention and diagnostic domains. Where there was a scarcity of Level I or Level II evidence, it was planned to expand the review to consider lower levels of evidence. Studies were limited to English language only.

Types of Participants

The review included research conducted in adults without pre-existing CVD or in those with and without CVD but where those without CVD were reported separately.

Types of Outcomes

In principle, the primary outcome for each question was cardiovascular events (definition for CVD as for the *Guidelines for the Assessment of Absolute Cardiovascular Disease Risk*). The secondary outcome of interest was absolute risk (AR) reduction, followed by surrogate outcomes such as individual risk factor reduction as specified in the questions (e.g., blood pressure [BP] control).

Search Strategy for Identification of Studies

A broad search strategy using the following databases and sources was used to identify potential studies:

- Medline
- EMBASE
- CINAHL
- PsycINFO
- Cochrane Library, including CENTRAL Cochrane Controlled Trial Register (CCTR) and DARE for some topics

In addition, the following websites were searched including Australian Centre for Clinical Effectiveness, National Institute for Health and Care Excellence, National Library for Health, Swedish Council on Technology Assessment in Healthcare, US Agency for Healthcare Research and Quality, and the US National Guideline Clearing House. The Expert Working Group (EWG) were sent interim search reports and asked to identify any additional studies.

Hand searching undertaken after the online database searching included the following journals: *British Medical Journal*, *New England Journal of Medicine*, *LANCET*, *Circulation*, *Journal of the American Medical Association*, *Archives of Internal Medicine*, *Medical Journal of Australia* and *Diabetes Care*.

The Cochrane library was also reviewed to incorporate new or updated reviews. Hand searching was undertaken to identify major meta-analyses or landmark trials to maximise the currency of the text. In one situation, literature identified after the comprehensive literature review period was deemed by the EWG to be sufficiently important to result in a change to the recommendations (i.e., BP targets for those with chronic kidney disease [CKD]). This decision took into consideration the quality of evidence (all high-quality meta-analyses), the need to provide clinicians with the most useful recommendation, alignment to draft international CKD guidelines, and the likely scenario that the current guidelines could be out of date before they were published.

In addition to the initial searches, economic literature was searched via EBSCO host database (Econlit & CINAHL), Ovid database (EMBASE, Medline), BioMed central and Cochrane library database (Health Technology Assessment, National Health Service Economic Evaluation). A broad search strategy of Australian and international literature (developed countries including European, North American and Canadian) for the years 2002–2010 was used. The cut-off dates build on the Scottish Intercollegiate Guidelines Network (SIGN) guidelines used during the systematic review phase.

Search Terms

Search terms were used for each group of clinical questions/topics. Search terms were based on those reported in the Supplementary Guidelines Material (SIGN) where the first series of strings are disease/population identifiers and the additional strings relate to the specific question, i.e., intervention (e.g., alcohol and euphemisms). Search strategies used in other databases were adjusted for different databases, but were substantially the same. Searches were combined with guidelines, systematic review, and trial filters as appropriate.

Study Selection

One reviewer assessed the titles and available abstracts of all studies identified by the initial broad searches (based on population and intervention) and excluded any clearly irrelevant studies. Two reviewers then independently assessed papers identified as potentially eligible studies using the inclusion criteria and resolved disagreements on inclusion by consensus, with reference to a third reviewer if necessary. This second phase thus focused on selection of studies based on the outcomes, treatment comparisons and any population subgroups (e.g., diabetes, CKD) which may have different effects of an intervention.

Hand searching identified 44 potential new trials or meta-analyses of which 9 were included in the final guidelines. During finalising of the guidelines two further meta-analyses on BP treatment in those with diabetes were identified and included.

Search terms used in the economic literature review were essentially the same for each database. A broad population identifier (CVD or cardiovascular disease OR coronary disease OR heart attack OR stroke) was used followed by the following terms: Exp "cost and cost analysis"; Costs. ti/ab; Cost effective$.ti/ab; Cost benefit analys$.ti/ab; Exp health care costs/; (economic adj2 evaluat$).ti/ab; and finally primary prevention. Additional snowballing searches were undertaken. The total number of hits was 204 of which 28 were considered in more detail by one member of the project team. Reviewing staff at Deakin University scrutinised the 16 abstracts for omissions and 9 additional appropriate papers were retrieved and reviewed.

The following criteria were used to select economic studies:

- Overseas evidence in developed countries of Europe, UK, North America, Canada
- AR of cardiovascular disease criteria
- Primary prevention population included has no previous history of CVD
- BP-lowering diuretics, beta blockers, calcium channel blockers (CCBs), angiotensin-converting enzyme (ACE) inhibitors
- Cholesterol-lowering medications statins
- Antiplatelets (aspirin)
- Adults 35–84
- Health outcome measured in disability-adjusted life-years (DALYs) or quality-adjusted life-years (QALYs)

See the technical report (see the "Availability of Companion Documents" field) for full details on inclusion, appraisal and summary of evidence.

Number of Source Documents

Refer to table 3.4 in Appendix 2 in the guideline for details of the search results for each of the guideline questions.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Designation of Levels of Evidence According to Type of Research Question

Level	Intervention	Diagnosis	Prognosis	Aetiology	Screening
I	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation	A prospective cohort study	A prospective cohort study	A randomised controlled trial
III-1	A pseudo-randomised controlled trial (i.e., alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation	All or none	All or none	A pseudo-randomised controlled trial (i.e., alternate allocation or some other method)
III-2	A comparative study with concurrent controls:	A comparison with a reference standard that does not meet the criteria required for Level II and Level III-1	Analysis of prognostic factors amongst untreated control	A retrospective cohort study	A comparative study with concurrent controls:

Level	Intervention	Diagnosis	Prognosis	Aetiology	Screening
	• Non-randomised experimental trial • Cohort study • Case-control study • Interrupted time series without a parallel control group	evidence	patients in a randomised controlled trial		• Nonrandomised, experimental trial • Cohort study • Case-control study
III-3	A comparative study without concurrent controls: • Historical control study • Two or more single arm studies • Interrupted time series without a parallel control group	Diagnostic case-control study	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: • Historical control study • Two or more single arm studies
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series or cohort study of patients at different stages of disease	A cross-sectional study	Case series

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence Tables

Data from included studies was abstracted along with a methodological appraisal (see below). This included information including citation, study type, evidence level (as per *National Health and Medical Research Council [NHMRC] Levels of Evidence and Grades for Recommendations for Developers of Guidelines [2009]*) patient number and characteristics, intervention/s, comparison, length of follow-up, outcome measure, effect size and funding source (as appropriate).

Methodological Quality Assessment

Two reviewers independently assessed the methodological quality of each included trial and resolved disagreements by consensus, with reference to a third reviewer if necessary. Methodological quality of existing guidelines was assessed using the Appraisal of Guidelines Research and Evaluation Collaboration (AGREE) instrument. Methodological quality of included systematic reviews and controlled trials was assessed using a

modified checklist based on the Scottish Intercollegiate Guidelines Network (SIGN) *Methodology checklist for systematic reviews and meta-analyses* and the Guidelines International Network draft evidence tables. These checklists were developed and used previously by the National Stroke Foundation (NSF). Methodological quality of included cohort studies was assessed using the SIGN *Methodology checklist for cohort studies*. For diagnostic studies identified, the SIGN *Methodological checklist for diagnostic studies* was used.

See the technical report (see the "Availability of Companion Documents" field) for full details on inclusion, appraisal and summary of evidence.

Methods Used to Formulate the Recommendations

Expert Consensus (Consensus Development Conference)

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

These guidelines were developed according the standards outlined in the *National Health and Medical Research Council (NHMRC) Standards and Procedures for Externally Developed Guidelines (2007)*.

Clinical Questions

The clinical questions were initially framed by building on the work undertaken in the development of the *Guidelines for the Assessment of Absolute Cardiovascular Disease Risk*. Further refinement was undertaken after consultation with international guidelines groups in Scotland and New Zealand. Questions were then grouped under topics and circulated to experts for comment. Some experts were consulted individually for further detailed comments. In response to the comments from experts, the questions were modified for further discussion and final approval at a face-to-face meeting of the Advisory Committee held on 26 November 2009.

The clinical questions are outlined in Appendix 2 of the original guideline document.

Formulation of Recommendations

To assist in the formulation of recommendations, where a body of evidence exists for each question, the NHMRC Grades process has been applied. This has resulted in an Evidence Statement for each question. The project team including the chair of the Expert Working Group (EWG), along with input of individual members of the EWG or corresponding group, used these statements and the underlying evidence to draft recommendations. The draft recommendations along with the summary matrices were initially discussed by the EWG at a face-to-face meeting of the working group on 7 September 2010. In addition to the summary matrices, economic modelling on the cost benefit of various drug therapies was commissioned and used to inform the development of the recommendations. Subsequent meetings via teleconferences were undertaken followed by a modified Delphi process (over two rounds) to achieve consensus (defined as >75% of responses from EWG) of the final wording of the recommendations. The recommended grading matrix was used to guide the strength of the recommendation.

Link between Research and Recommendations Following an Absolute Risk (AR) Approach

These guidelines take an AR approach to the management of cardiovascular disease (CVD) risk which has posed some challenges in formulation of the recommendations. This is because although there is robust and compelling evidence in the published literature which clearly shows that pharmacotherapy reduces the levels of individual risk factors (blood pressure and lipids) with consequent reduction in CVD mortality or CVD events, this evidence is based on a single risk factor/relative risk approach. Therefore the expert panel carefully considered the literature before making and grading the recommendations in an AR paradigm. When examining the evidence, consideration was given to any heterogeneity found between subgroups and the generalisability of the findings. The final grading of these recommendations was downgraded to account for the uncertainty of applying evidence from a relative risk approach to an AR paradigm.

Reporting of Study Results

Study results have been reported in the text of these guidelines in the same form as reported in the research, i.e., where relative risk reduction has been the measure used in the study, the results are reported using this term and have not been converted to AR reduction.

Additional Guidance

Where no robust evidence was found for the search questions, the EWG followed the consensus process to develop consensus-based recommendations. Practice points were provided to give practical guidance to facilitate the implementation of the guidelines.

Guidelines Text

The body of the text was drafted by a consultant medical writer (medScript) based on an agreed framework. Early drafts were circulated for input from the EWG and finalised by the project team for public consultation.

Rating Scheme for the Strength of the Recommendations

Grading of Evidence-based Recommendations (EBR)

Grade of Recommendation	Description
A	Body of evidence can be trusted to guide practice.
B	Body of evidence can be trusted to guide practice in most situations.
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application.
D	Body of evidence is weak and recommendation must be applied with caution.

Additional Guidance

CBR	Consensus-based recommendations: developed by the guidelines expert working group when a systematic review of the evidence found either an absence of direct evidence which answered the clinical question or poor quality evidence, which was deemed not to be strong enough to formulate an evidence-based recommendation.
PP	Practice points: developed by the guidelines expert working group where a systematic review had not been conducted but there was a need to provide practical guidance to support the implementation of the evidence-based and/or consensus-based recommendations.

Cost Analysis

See Appendix 3 in the original guideline document for economic considerations.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

These guidelines were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on 27 April 2012, under Section 14A of the National Health and Medical Research Council Act 1992. In approving these guidelines the NHMRC considers that they meet the NHMRC standard for clinical practice guidelines. This approval is valid for a period of 5 years.

Consultation

Correlation with the Draft *National Evidence-Based Guideline on Secondary Prevention of Vascular Disease in Type 2 Diabetes*

These guidelines were developed at the same time as the *National Evidence-Based Guideline on Secondary Prevention of Vascular Disease in Type 2 Diabetes* (currently being drafted). The two groups consulted extensively to ensure that the two guidelines provided a consistent continuum of care for patients (including cross representation on each advisory committee). As far as possible, given the evidence available for the different populations, the guidelines are consistent. Where there are differences in the grading of recommendations, this is due to the difference in evidence for the two populations.

Public Consultation

In line with the requirement under Section 14A of the National Health and Medical Research Council Act 1992, the public consultation process invited feedback during a month-long period in April 2011 and included an advertisement in the press inviting public comment. In addition, a notice of the opportunity for comment was posted on the websites of National Vascular Disease Prevention Alliance (NVDPA) member organisations and copies of the guidelines were distributed to a broad group of identified stakeholders and networks. Consumer organisations were also contacted for comment. Finally, the draft document was circulated via the networks of the various experts supporting the project. Five prompted questions, modified from key questions included in the Guidelines Implementability Tool, were also included in the consultation feedback form to provide general feedback.

Overall there were 388 individual comments received from 24 individuals and 19 organisations (including key organisations such as the Royal Australian College of General Practitioners, Stroke Society of Australasia, state health departments, Australian General Practice Network and the Cardiac Society of Australia and New Zealand). Public consultation resulted in many detailed responses, including many positive comments. The major contentious issues and changes made in response to the public consultation can be found in the original guideline document.

Evidence Supporting the Recommendations

References Supporting the Recommendations

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Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Where no robust evidence was available but there was sufficient consensus within the Expert Working Group (EWG), consensus-based recommendations (CBR) have been provided. Practice points (PP) were added where necessary, to provide practical guidance to facilitate the implementation of the guidelines.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- There is emerging evidence that clinical decisions based on absolute cardiovascular disease (CVD) risk may lead to improved management of CVD risk. Access to absolute CVD risk assessments has been shown to increase prescribing of lipid-modifying drugs for high-risk people with diabetes and lead to improvement in lipid profiles and significant reductions in the risk of coronary heart disease (CHD). As absolute CVD risk assessment provides a more accurate assessment of risk than individual risk factors, it is reasonable to expect that basing management decisions on this assessment will improve outcomes.
- At the population level, interventions targeting those at highest overall CVD risk are likely to achieve the best balance between preventing death and avoiding unnecessary treatment in those at lower risk. For example, lipid-lowering treatment in people assessed to be at high risk on consideration of all risk factors present will potentially prevent twice as many deaths from CHD in a given population than treating only those with total cholesterol levels above a given arbitrary cut-point. Therefore, accurate estimation of CVD risk, especially in people without known CVD, could play a complementary role with other strategies (e.g., to reduce salt and tobacco consumption) in delivering effective population preventive health programs. Since the mid-1990s, major guidelines for the prevention of CVD have moved from an approach based on identifying and correcting individual risk factors through the application of several separate guidelines, to a focus on the individual's overall risk through multiple risk factor assessment.

Potential Harms

Adverse effects of pharmacotherapy. All patients started on a statin should be advised to report unexplained muscle pains or other adverse effects promptly, especially if associated with fever or malaise. If such effects are mild, a different statin may be tried and/or the statin dose reduced after discussing the risks involved with the patient. If severe side effects are experienced, statin therapy should be discontinued.

Risks of Treatment

For all individuals, a clinical judgment should be made to assess the balance between the benefits and risks of pharmacological treatment. Clear benefits in preventing cardiovascular events and reducing premature mortality have been demonstrated for blood pressure and lipid-lowering therapy in many clinical trials. However not all clinical situations in which their use may be considered have been covered by clinical trials, e.g., in the elderly.

Use of these therapies is associated with risks and other negative effects which should be taken into consideration when deciding the appropriateness of implementing the treatment recommendations contained in these guidelines. These therapies may be contraindicated in some situations and their use may result in troublesome side effects. In addition, polypharmacy may be unaffordable to some, may increase the risk of side effects and may impact on quality of life.

The appropriateness of general treatment targets to the individual should also be considered. Cardiovascular disease risk associated with lipid and blood pressure levels is continuous and specific targets are somewhat arbitrary and should be used as a guide to treatment and not as a requirement, especially if they cannot be easily achieved without causing unwanted effects. The risks associated with the effort required to reach a particular target as opposed to achieving a near-target value may outweigh any small absolute benefit. Any reduction in a risk factor will be associated with some benefit.

Qualifying Statements

Qualifying Statements

- This document is a general guide to appropriate practice, to be followed subject to the circumstances, clinician's judgement and patient's preferences in each individual case. The guidelines are designed to provide information to assist decision making and are based on the best available evidence at the time of development. The relevance and appropriateness of the information and recommendations in this document depend on individual circumstances. Moreover, the recommendations and guidelines are subject to change over time. While all care has been taken in preparing the content of this material, the National Vascular Disease Prevention Alliance and the funding body expressly disclaims and accepts no responsibility for any undesirable consequences arising from relying on the information or recommendations contained herein.
- This publication reflects the views of the authors and not necessarily the views of the Australian Government.

Implementation of the Guideline

Description of Implementation Strategy

Implementation Considerations

Background

The National Vascular Disease Prevention Alliance (NVDPA)'s new *Guidelines for the Management of Absolute Cardiovascular Disease Risk* is an important step along the path to improved prevention of cardiovascular disease (CVD) in Australia. Of greater importance is the dissemination and application in practice. Like the guidelines themselves, implementation strategies should use an evidence-based approach based on an underlying framework for CVD prevention. In addition to the various NVDPA guideline development groups, establishment of this plan was enhanced by obtaining structured feedback at a meeting of key stakeholders (46 government, non-government, consumer and professional organisation representatives) on 3 March 2011. This meeting was called to specifically address implementation considerations from a broad range of perspectives.

Strategic Framework

These guidelines are one important part of a coordinated strategic framework for improving CVD prevention in Australia. This framework includes activities at an individual and population level to raise awareness of CVD risk, assess risk and manage risk to prevent CVD as outlined in the diagram (see "Implementation" section in Appendix 2 of the original guideline document). These guidelines focus only on comprehensive risk assessment and management aimed at primary prevention of CVD. Therefore, the guidelines and implementation strategies should not be considered as a standalone process but need to be linked to other important strategies both at an individual and population level to maximise their impact.

Levels to Consider When Implementing Guidelines

Local factors operate over several different levels; all need to be considered to maximise the effect of guidelines. These levels are broadly described into four main categories: professional, organisational, consumers and regulatory/financial. Strategies to address barriers identified at

each of these levels need to be developed. Strategies that enhance enabling factors should also be created. These are briefly described below:

1. Professional level: strategies supporting health professionals to adopt recommendations in the guidelines. Strategies include:
    a. Dissemination/distribution of the guidelines
    b. Education and training
    c. Audit and feedback, reminders or decision support tools
    d. Use of local consensus processes
2. Organisational level: strategies supporting organisational change to facilitate adoption of the guidelines. Such strategies may include quality improvement systems, accreditation processes, adoption of policies and protocols.
3. Consumer level: strategies supporting behaviour change among consumers in relation to the guidelines.
4. Regulatory or financial level: strategies targeting regulatory systems to support change at all levels. This may include change in reimbursement items for general practitioners, incentives, approval and cost of medicines.

Evidence-based Implementation of Clinical Guidelines

Several systematic reviews of evidence for guidelines implementation have been undertaken. While most strategies have been found to lead to small to moderate improvement (e.g., 5%–10%) there is no simple or single strategy that will apply in all settings. However methodological weaknesses and poor reporting of the study setting and uncertainty about the generalisability of the results limit the strength of the conclusions.

It is suggested that strategies to implement the guidelines will be most effective where a concrete plan is developed that tailors specific strategies based on an analysis of local factors necessary for clinical behaviour change. Such factors include assessment of both the barriers and enablers to achieving the recommendations in the clinical guidelines. More than one approach is often needed to overcome barriers because these occur at different operational levels within the health system. These levels are discussed above.

Evidence (generally focused on changes at the professional level) from recent systematic reviews indicates:

- Audit and feedback produce small to modest improvements in adherence to evidence-based care from a large number of wide ranging studies. However, quality-improvement activities often use a multifaceted strategy such as educational meetings, reminders, printed material or opinion leaders with or without audit and feedback.
- Educational meetings alone are not likely to be effective for changing complex behaviours but can be effective if used with other interventions.
- Inter-professional collaboration (collaboration between professionals within and across locations) may have a positive effect in patient outcomes.
- Interventions tailored to identified barriers (for example, through interactive group work) are more likely to improve professional practice than no intervention or dissemination of guidelines alone.
- Printed education materials may have some benefits compared with no material but the effect is unclear compared with other interventions.
- Local opinion leaders can successfully reduce non-compliance with evidence-based practice.
- Quality improvement collaboratives may have some benefit, but the evidence for this, although positive, was limited. However, this approach has been successfully utilised by the Australian Primary Care Collaboratives (APCC) to improve best-practice care for diabetes and chronic heart disease in general practice.

Recommended Implementation Activities

Considering the evidence for guideline implementation, strategies to implement the *Guidelines for the Management of Absolute Cardiovascular Disease Risk* will need to be chosen based on the target audience and level of focus (e.g., professional, organisational, consumer or regulatory/financial level). Each strategy will need to consider potential barriers (or enablers) and be tailored to address identified factors. Some initial examples are provided below.

Consultation with stakeholders and a review of the evidence has led to potential examples of barriers, enablers and possible solutions for each level to be considered when implementing the guidelines.

Refer to Appendix 2 in the original guideline document for additional information on implementation activities.

Implementation Tools

Clinical Algorithm

Patient Resources

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Vascular Disease Prevention Alliance. Guidelines for the assessment of absolute cardiovascular disease risk. Canberra (Australia): National Stroke Foundation (Australia); 2012 May. 123 p. [359 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2009 (revised 2012 May)

Guideline Developer(s)

National Stroke Foundation (Australia) - Nonprofit Organization

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Guideline Committee

Expert Working Group

Composition of Group That Authored the Guideline

Expert Working Group Members: Professor Stephen Colagiuri (*Chair*), Diabetologist, Boden Institute of Obesity, Nutrition, Exercise and Eating Disorders, The University of Sydney; Professor Andrew Tonkin, Cardiologist, Cardiovascular Research Unit, Monash University; Professor Leonard Arnolda, Cardiologist, Canberra Hospital and Australian National University; Professor Alex Brown, Indigenous Health, Executive Director and Margaret Ross Chair of Indigenous Health, Baker IDI Central Australia; Professor Terry Campbell, AM, Cardiologist (PBAC representative), University of New South Wales; Professor Derek Chew, Cardiologist, Flinders University; Dr David Dunbabin, Stroke Specialist/Geriatrician, Royal Hobart Hospital and University of Tasmania; Professor Mark Harris, General Practitioner, Centre for Primary Health Care and Equity, University of New South Wales; Professor David Johnson, Nephrologist, Princess Alexandra Hospital and University of Queensland; Mr Richard McCluskey, Consumer representative; Professor Mark Nelson, General Practitioner, Menzies Research Institute of Tasmania, University of Tasmania; Associate Professor David Sullivan, Clinical Biochemistry, Royal Prince Alfred Hospital and University of Sydney

Financial Disclosures/Conflicts of Interest

A policy regarding disclosure and management of potential conflicts of interest (COI) was implemented. All Advisory Committee and Expert Working Group (EWG) members completed COI forms and a COI register was maintained and updated regularly. COI were managed in the following manner:

- Open disclosure of all COI to all members of the committee and public declaration of all COI in guidelines.
- If the COI is deemed significant, individuals may be restricted from involvement in discussions and decisions on related topics. This is determined by the chair of the relevant committee and has occurred once.
- If the COI is considered exclusionary, the individual will be excluded from membership of the relevant committee or from employment in the guidelines team. This will be determined by the chair of the relevant committee and the Chief Executive Officer (CEO) of the National Stroke Foundation, the lead agency for this project. This level of COI has been experienced and the relevant member resigned from the committee.

A copy of the Conflict of Interest Policy can be supplied on request.

Guideline Endorser(s)

Royal Australian College of General Practitioners - Professional Association

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Vascular Disease Prevention Alliance. Guidelines for the assessment of absolute cardiovascular disease risk. Canberra (Australia): National Heart Foundation of Australia; 2009. 49 p. [118 references]

Guideline Availability

Electronic copies: Available from the National Stroke Foundation (Australia) Web site .

Availability of Companion Documents

The following are available:

- National Vascular Disease Prevention Alliance. Absolute cardiovascular disease risk management. Inclusion, appraisal and summary of evidence for the National evidence-based guideline for the management of absolute cardiovascular disease risk. Technical report. Canberra (Australia): National Stroke Foundation (Australia); 2012. 412 p. Electronic copies: Available from the National Stroke Foundation (Australia) Web site .
- National Vascular Disease Prevention Alliance. Quick reference guide for health professionals. Absolute cardiovascular disease risk management. Canberra (Australia): National Stroke Foundation (Australia); 2012. 8 p. Electronic copies: Available from the National Stroke Foundation (Australia) Web site .
- National Vascular Disease Prevention Alliance. 10 Things to know about the Guidelines for the Management of Absolute Cardiovascular Disease Risk (2012). Canberra (Australia): National Stroke Foundation (Australia); 2012. 1 p. Electronic copies: Available from the National Stroke Foundation (Australia) Web site .
- Australian absolute cardiovascular disease risk calculator. 2014. Available from the National Stroke Foundation (Australia) Web site .
- Absolute risk videos. Available from the Heart Foundation (Australia) Web site .

Patient Resources

The following is available:

- Manage your heart and stroke risk. A 3-step guide to better health. Consumer booklet. 2012. 8 p. Electronic copies: Available from the National Stroke Foundation (Australia) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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